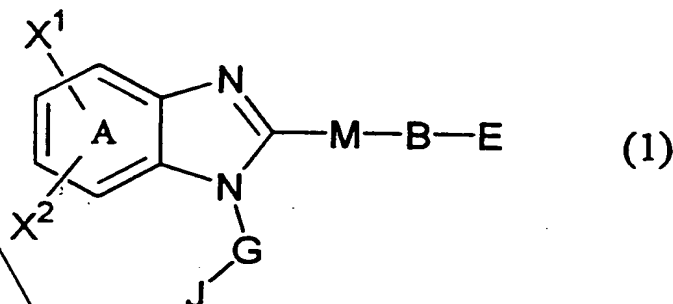


CLAIMS

1. An inhibitor against human chymase activity containing a benzimidazole derivative expressed by the following formula (1) or its salt as an active ingredient,



[in the formula (1), the ring marked with A expresses a pyridine ring or a benzene ring;

X¹ and X² are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a hydroxyl group, a nitro group, a cyano group, -CH₂NH₂, -CH=NR¹, -CH=NOR¹ or -CONR¹R² (here, R¹ and R² are each a hydrogen atom or a C₁₋₄ alkyl group), -COOR³ (here, R³ is a hydrogen atom or a C₁₋₄ alkyl group), a substituted or unsubstituted C₁₋₆ normal, cyclic or branched alkyl group, a substituted or unsubstituted C₃₋₇ cycloalkyl group, a substituted or unsubstituted C₁₋₆ normal or branched alkoxy group, a substituted or unsubstituted C₁₋₆ normal or branched alkylthio group, a substituted or unsubstituted C₁₋₆ normal or branched alkylsulfonyl group or a substituted or unsubstituted C₁₋₆ normal or branched alkylsulfinyl group (the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s));

B is a substituted or unsubstituted C₁₋₆ normal, cyclic or branched alkylene group or a substituted or unsubstituted C₂₋₆ normal or branched alkenylene group (the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C₁₋₆ normal or branched alkoxy

group (including the case where adjacent two groups form an acetal bonding), a C₁₋₆ normal or branched alkylthio group, a C₁₋₆ normal or branched alkylsulfonyl group, a C₁₋₆ normal or branched acyl group, a C₁₋₆ normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s) of the alkylene group or an alkenylene group; between atoms, the alkylene group or alkenylene group optionally contains one or more of -O-, -S-, -SO₂- or -NR⁴-, but this atom or atomic group does not bond directly to the M, and here R⁴ is a hydrogen atom or a C₁₋₆ normal or branched alkyl group};

E expresses -COOR⁴, -SO₃R⁴, -CONHR⁵, -SO₂NHR⁴, -PO(OR⁶)₂, a tetrazol-5-yl group, a 5-oxo-1,2,4-oxadiazol-3-yl group or a 5-oxo-1,2,4-thiadiazol-3-yl group (here, R⁴ is similarly defined as above; R⁵ is a hydrogen atom, a cyano group, or a C₁₋₆ normal or branched alkyl group; R⁶ is a hydrogen atom, a C₁₋₆ normal or branched alkyl group, or trifluoromethylsulfonyl group, or its pharmaceutically permissible salt);

G is a substituted or unsubstituted C₁₋₆ normal or branched alkylene group (between atoms, the alkylene group optionally contains one or more of -O-, -S-, -SO₂- or -NR⁴-, but this atom or atomic group does not bond directly to the nitrogen atom of the imidazole ring (R⁴ is similarly defined as above), and the substituent is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C₁₋₆ normal or branched alkoxyl group (including the case where adjacent two groups form an acetal bonding), a trihalomethyl group, a trihalomethoxy group, a phenyl group or an oxo group};

J is a substituted or unsubstituted C₁₋₆ normal, cyclic or branched alkyl group, a substituted or unsubstituted C₄₋₁₀ aryl group (the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, -COOR⁷ (here, R⁷ is a hydrogen atom or a C₁₋₄ alkyl group), a C₁₋₆ normal, cyclic or branched alkyl group, a C₁₋₆ normal or branched alkoxyl group (including the case where adjacent two groups form an acetal bonding), a C₁₋₆ normal or branched alkylthio group, a C₁₋₆ normal or branched alkylsulfonyl group, a C₁₋₆ normal or branched alkylsulfinyl group, a C₁₋₆ acyl group, a C₁₋₆ normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy

SUB
A2
C004

10

~~st human chyr~~
~~A in the above~~
~~st human chyr~~
~~A in the above~~

wherein the ring marked with A in the above formula (1) is a pyridine ring.

15

20



25

sub
A2

alkoxyl group, a substituted or unsubstituted C₁₋₃ normal or branched alkylthio group, a substituted or unsubstituted C₁₋₃ normal or branched alkylsulfonyl group, or a substituted or unsubstituted C₁₋₃ normal or branched alkylsulfinyl group; there is no limitation regarding the substitution positions of X³, X⁴ and X⁵ on the benzene ring or the naphthalene ring].

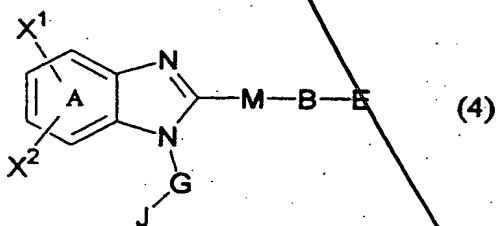
6. An inhibitor against human chymase activity set forth in one out of Claims 1 to 5 wherein M in the above-mentioned formula (1) is a sulfur atom.

7. An inhibitor against human chymase activity set forth in one out of Claims 1 to 6 wherein B in the above-mentioned formula (1) is a substituted or unsubstituted C₁₋₆ normal, cyclic or branched alkylene group.

8. An inhibitor against human chymase activity set forth in one out of Claims 1 to 7 wherein G in the above-mentioned formula (1) is -CH₂-, -CH₂CH₂-, -CH₂CO-, -CH₂CH₂O-, -CH₂CONH-, -CO-, -SO₂-, -CH₂SO₂-, -CH₂S- or -CH₂CH₂S- (J bonds to the right side of said group).

9. An inhibitor against human chymase activity set forth in one out of Claims 1 to 8 wherein E in the above-mentioned formula (1) is -COOH.

10. A benzimidazole derivative expressed by the following formula (4) or its pharmaceutically permissible salt,



[in the formula (4), the definitions of the ring marked with A, and X¹, X², B, E, G, J and M are same as those in the above formula (1); however, excepting the case where at least one of X¹ and X² is a cyano group, -CH₂NH₂, -CH=NR¹, -CH=NOR¹ or -CONR¹R² (here, R¹ and R² are each a hydrogen atom or a C₁₋₄ alkyl group), J expresses only a substituted naphthalene ring].

11. A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 10 wherein X¹ and X² in the above formula (4) are each a hydrogen atom, a cyano group, -CH₂NH₂, -CH=NR¹, -CH=NOR¹ or -CONR¹R² (here, R¹ and R² are each a hydrogen atom or a C₁₋₄ alkyl group; X¹ and X² are not hydrogen at the same time).

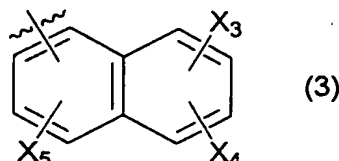
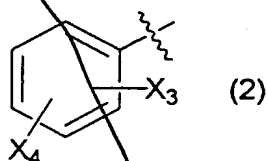
12. A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 10 wherein X^1 and X^2 in the above formula (4) are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a hydroxyl group, a nitro group, $-CH=NR^1$ (here, R^1 is a hydrogen atom or a C_{1-4} alkyl group), $-COOR^3$ (here, R^3 is a hydrogen atom or a C_{1-4} alkyl group), a substituted or unsubstituted C_{1-6} normal, cyclic or branched alkyl group, a substituted or unsubstituted C_{3-7} cycloalkyl, a substituted or unsubstituted C_{1-6} normal or branched alkoxy group, a substituted or unsubstituted C_{1-6} normal or branched alkylthio group, a substituted or unsubstituted C_{1-6} normal or branched alkylsulfonyl group or a substituted or unsubstituted C_{1-6} normal or branched alkylsulfinyl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s)}.

13. A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 10 wherein X^1 and X^2 in the above formula (4) are each a hydrogen atom or a cyano group (here, X^1 and X^2 can not be hydrogen atoms at the same time).

14. A benzimidazole derivative or its pharmaceutically permissible salt set forth in one out of Claims 10 to 13 wherein M in the above formula (4) is a sulfur atom.

15. A benzimidazole derivative or its pharmaceutically permissible salt set forth in one out of Claims 10 to 14 wherein B in the above formula (4) is a substituted or unsubstituted C_{1-6} normal, cyclic or branched alkylene group.

16. A benzimidazole derivative or its pharmaceutically permissible salt set forth in one out of Claims 10 to 15 wherein J in the above formula (4) is a group expressed by the following formula (2) or (3),



[here, X³, X⁴ and X⁵ are each at the same time or independently a hydrogen atom, a halogen atom, a hydroxyl group, a nitro group, a cyano group, a trihalomethyl group, a trihalomethoxy group, -COOR⁷ (here, R⁷ is a hydrogen atom or a C₁₋₄ alkyl group), a substituted or unsubstituted C₁₋₃ normal or branched alkyl group, a substituted or unsubstituted C₁₋₃ normal or branched alkoxyl group, a substituted or unsubstituted C₁₋₃ normal or branched alkylthio group, a substituted or unsubstituted C₁₋₃ normal or branched alkylsulfonyl group, or a substituted or unsubstituted C₁₋₃ normal or branched alkylsulfinyl group; there is no limitation regarding the substitution positions of X³, X⁴ and X⁵ on the benzene ring or the naphthalene ring].

17. A benzimidazole derivative or its pharmaceutically permissible salt set forth in one out of Claims 10 to 16 wherein G in the above formula (4) is -CH₂-, -CH₂CH₂-, -CH₂CO-, -CH₂CH₂O-, -CH₂CONH-, -CO-, -SO₂-, -CH₂SO₂-, -CH₂S- or -CH₂CH₂S- (J bonds to the right side of said group).

18. A benzimidazole derivative or its pharmaceutically permissible salt set forth in one out of Claims 10 to 17 wherein E in the above formula (4) is COOH.

19. A pharmaceutical composition consisting of a benzimidazole derivative and/or its pharmaceutically permissible salt set forth in one out of Claims 10 to 18, and a pharmaceutically permissible carrier.

20. A chymase activity inhibitor set forth in one out of Claims 1 to 9 whose targeting disease is an inflammatory disease, an allergy disease, a respiratory disease, a cardiovascular disease or a bone/cartridge metabolic disease.

21. A human chymase activity inhibitor set forth in Claim 20 which is a preventing agent or a treating agent of a disease.